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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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AKIN, GUMP, STRAUSS, HAUER & FELD, L.L.P.
ONE COMMERCE SQUARE
2005 MARKET STREET, SUITE 2200
PHILADELPHIA, PA 19103

EXAMINER	
HAYES, ROBERT CLINTON	
ART UNIT	PAPER NUMBER
1647	9

DATE MAILED: 04/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/596,507	Peschel
Examiner	**Art Unit**
Robert C. Hayes, Ph.D.	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 16, 2002*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *26-43* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *26-43* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *4, 5 & 8*

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election without traverse of Group I (original claims 1-10 & 24-25) in Paper No. 7 is acknowledged. Because it appears that Applicant's invention is now only directed toward a mixed population of neuronal progenitor cells actively differentiating into dopaminergic neurons, along with the differentiated dopaminergic neurons themselves, the neuronal progenitor cells and the differentiated neuron population will not be further restricted into their respective distinct group, unless later claimed as such.

Claim Objections

2. Claims 29-30, 32-33, 34-35, 38-39 & 42 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. .

Base claims 26 & 34 are directed toward neuronal progenitor cells and differentiated dopaminergic neurons. The recitations "derived from immature progenitor cells...", or "progenitor cells" alone, or "monoclonal progenitor cell lines" are broader than base claims 26 and 34, because glial progenitor cells, etc., also exist. Additionally, "immature progenitor cells" cannot also be differentiated dopaminergic neurons, as recited.

3. Claims 37 is objected to because of the following informalities: "interleukines" and "interferones" are misspelled, and which "IL1-16" should be "IL 1- IL 16". Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No proper antecedent basis nor conception within context of that described within the specification is apparent for the current recitation of ">90%... neuronal progenitor cells/progenitor cells" (i.e., as it relates to claims 26-27 & 35), or for "wherein at least one of the steps... is repeated" (i.e., as it relates to claim 36 versus the specific series of steps recited in original claim 11), or for the additional method steps recited in the second, third and forth paragraphs of base claim 34, etc., or for "conditions *simulating induced* oxygen content" (i.e., as it relates to claim 41), or for "being *adapted* for transplantation to restore neuronal deficits" (i.e., as it relates to claim 31); thereby constituting new matter.

5. Claims 26-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds for "not containing any *physiologically active* amounts of *immunocompetent* glial cells" are unknown nor described, while also being ambiguous as to what exactly is envisioned to be claimed (i.e., as it relates to claim 26). In other words, how are "physiologically active amounts", immunocompetency and glial cells suppose to be related, if at all? Cells either invoke an immune reaction, or they do not.

The metes and bounds of what constitute "tissue material and differentiating promoting factor", or "exogenous factors", are unknown and ambiguous since none are specifically recited (i.e., as it relates to claims 26-27, 34-35 & 42).

It is unclear what the "*issue* according to claim 26" entails when no "issue" is mentioned in base claim 26; thereby, being indefinite (i.e., as it relates to claim 27).

6. Claims 31-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and incomplete for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds envisioned by the recitation of "being *adapted* for transplantation to restore neuronal deficits" are unknown and unclear; especially when no "neuronal deficits" to

be "restored" are recited (i.e., as it relates to claims 31 & 43); thereby, also being an incomplete method.

The second, third and forth paragraphs of base claim 34 make little sense and are confusing, in that "proliferation of selected progenitor cells..." should not be occurring after "partial differentiation", and "wherein at least one step of the partial differentiation" should not be occurring after 'subcloning", if the individual recited steps recited in the first paragraph are being followed. Second, it is unclear where the later recited "priming-step", "subsequent selection and proliferation" step, "differentiating" step, "partial differentiation" and then "differentiation" step occur. It is further ambiguous how "re-differentiation" is expected to occur, because cells are either differentiated, or they are not; or exactly what is envisioned by this recitation.

Subcloning of differentiated cells makes no sense, since these cells no longer proliferate, by definition; thereby, being indefinite and ambiguous (i.e., as it relates to claim 34).

No proper antecedent basis exists in claims 36 & 39 for the recitation of "at least one of the steps selected from the group consisting of", because multiple steps are already recited in base claim 34 (which further do not include the step of "expansion" as recited in claim 39); thereby, making it impossible to determine what exact steps are envisioned to be "repeated".

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 26-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Boss et al. (US Patent 5,411,883; IDS Ref #3).

Boss et al. teach isolation of human and porcine neuron progenitor cells (e.g., mammalian brain-derived neuronal tissue from the mesencephalon that inherently contain progeny of a single multipotent neural stem cell derived from immature progenitor cells; thereby, being a monoclonal cell line in the broadest sense (cols. 3-7; as it relates to claims 26, 28, 29, 30 & 34). Columns 6-9 describe dissection, isolation of progenitor cells and proliferation of progenitor cells. Partial differentiation, full differentiation and selecting individual cells expressing dopaminergic markers are described in columns 13 & 20 (i.e., as it relates to claim 34). Proliferating the neural cells in fresh F12 medium + either 5% fetal cord serum (i.e., tissue material; as it relates to claims 26-27 & 34-35), or 5% Chang's supplement C, in which either medium inherently contain cytokines/ exogenic factors, meets the limitations of claims 34, 37 & 42. In that these cells were transplanted and survived the procedure up to 4 weeks post-grafting, the limitations of claims 31-33 & 43 are anticipated, as well as the limitations of "not contain[ing] any physiologically active amounts of immuno-competent glial cells" in base claims

29 & 34, because no graft rejection/immuno-response was observed nor mentioned by Boss et al.; absent evidence to the contrary. Continued culturing of these differentiated dopaminergic cells in the presence of 5 mM dbc-AMP for one week resulted in more catecholamine production and different proportions of catecholamine production, as determine by HPLC analysis (i.e., a dopaminergic marker; col. 20; as it relates to repeated proliferation, selecting and differentiation in claim 36), which lastly now reasonably contains >90% dopaminergic neurons; absent evidence to the contrary (i.e., as it relates to claims 27 & 35).

Of note is that the instant claims are directed toward the product of neuronal progenitor cells that are differentiating into dopaminergic neurons, and that neither the intended use nor the method of making such products carry any patentable weight; nor would such recitations obviate the rejections made of record (i.e., as it especially relates to claims 29, 30, 31-32 & 34-43).

8. Claims 26-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Emory University/Luskin et al. (WO 97/02049; IDS Ref #10).

Luskin et al. teach isolation of human and mammalian brain-derived neuronal progenitor cells capable of differentiating into >90% dopaminergic neurons (e.g., pgs. 3, 7, 9, 11, 14 & 29; as it relates to claims 26-28 & 34-35). Luskin's progenitor cells contain less than 5%, and even less than 2% glial cells (i.e., including "immuno-competent glial cells"), as described on pages 8, 11 & 21 (i.e., as it relates to base claims 26 & 34). In that cells from the SVZa (anterior subventricular zone) contain neuronal progenitor cells (e.g., pages 6, 7 & 9), which are

"immature progenitor cells", by definition, and inherently are progeny of a single multipotent neural stem cell, the limitations of claims 29 & 32, as well as the limitations of a monoclonal cell line in the broadest sense (i.e., as it relates to claims 30, 33 & 38), are anticipated. Alternatively, monoclonal cell lines are described on pages 37-38 (i.e., as it relates to claims 30, 33 & 38). Pages 9, 11, 12, 17-22 then describe dissection, isolation of progenitor cells and proliferation of neuronal progenitor cells. Partial differentiation, full differentiation and selecting individual cells expressing dopaminergic markers is also described, for example, on pages 12, 14, 16 & 29 (i.e., as it relates to claim 34). Proliferating the neural cells in Ham's F10 medium or DMEM supplemented with 10% fetal calf serum (i.e., tissue material), anticipates claims 26-27 & 34-35, in which this medium inherently also contains cytokines/ exogenic factors (i.e., as it relates to claims 34 & 37). Growth factors/cytokines/exogenous factors to be used for proliferation or for priming differentiation are described on pages 10, 12 & 15 (i.e., as it relates to claims 26-27, 34-35, 37 & 42). Lastly, in that these cells were transplanted to restore neuronal function, the recitation that they are "capable of restoring neuronal deficits following transplantation" is met (e.g., pgs 12-13, 18 & 29; as it relates to claims 31-33 & 43).

Of note is that the instant claims are directed toward the product of neuronal progenitor cells that are differentiating into dopaminergic neurons, and that neither the intended use nor the method of making such products carry any patentable weight; nor would such recitations obviate the rejections made of record (i.e., as it especially relates to claims 29, 30, 31-32 & 34-43).

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
April 3, 2002

GARY L. KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600